

APPLICATION FOR LETTERS PATENT

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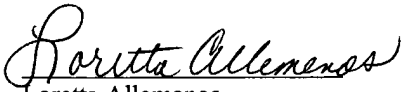
HIGH POLARIZATION FERROELECTRIC  
LIQUID CRYSTAL COMPOSITIONS

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## HIGH POLARIZATION FERROELECTRIC LIQUID CRYSTAL COMPOSITIONS

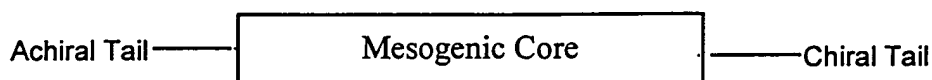
### BACKGROUND OF THE INVENTION

The present invention relates generally liquid crystal compounds and compositions and to optical devices employing liquid crystal compositions in optical switching and display elements. The invention more specifically relates to chiral nonracemic compounds useful as dopants in ferroelectric liquid crystal compositions to impart high polarization and fast switching speed. The dopants combine a rod-like mesogenic core with a chiral nonracemic tail and an achiral tail that comprises a perfluoroalkyl terminal portion.

The present invention relates to compounds useful as components in liquid crystal (LC) compositions, particularly as components of LC compositions that exhibit smectic phases and more particularly as components of LC compositions that exhibit smectic A and/or smectic C phases. LC compositions of this invention may also exhibit nematic phases. LC compositions of this invention can be ferroelectric liquid crystals (FLCs). The invention also relates to optical devices employing LC and FLC compositions of the invention in optical switching and display elements.

Several types of smectic liquid crystal materials (LCs) have been investigated for rapid switching, view-angle enhancement and higher contrast, including surface-stabilized ferroelectric LCs (FLCs), deformed helix ferroelectric LCs (DHFLCs), and antiferroelectric LCs (AFLCs). Recently, smectic material exhibiting thresholdless or more properly V-shaped switching LCs (VLCs) have been described (Inui, S. et al. (1996) J. Mater. Chem. 6(4):671-673; Seomun, S.S. et al. (1997) Jpn. J. Appl. Phys. 36:3580-3590).

Liquid crystal (LC) compositions exhibit one or more LC phases. LC compositions may be composed of one or more components. Components of LC compositions may exhibit liquid crystal phases, have latent liquid crystal phases or be compatible with (not suppress) liquid crystal phases in the LC composition. LC compounds and components of LC mixtures of this invention are rod-like molecules most typically having a generally linear mesogenic core with one or more directly or indirectly linked alicyclic or aromatic rings (which may be fused aromatic rings) and linear or branched tail groups distributed on either side of the mesogenic core, e.g.:



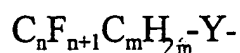
LC components which do not themselves exhibit liquid crystal phases, but which exhibit LC phases on combination with one or more other components are described as having "latent" liquid crystal phases. Chiral nonracemic LCs useful in FLC, DHFLC, AFLC and VLC compositions have at least one component that has a chiral nonracemic tail group. FLC, DHFLC, AFLC and VLC compositions may be composed entirely of chiral non-racemic components, but are typically composed of a mixture of chiral nonracemic and achiral or racemic components.

Ferroelectric LCs when aligned parallel to the substrate surfaces using the surface stabilized effect (in an surface-stabilized ferroelectric liquid crystal (SSFLC) device) exhibit two stable state switching on a microsecond time scale. Antiferroelectric LCs exhibit three stable-state switching, which by application of a bias field can be converted for use in a bistable switching mode LC devices. Two of the AFLC states have the same transmittance, so that alternate symmetrical switching can be used in AFLC devices. VLCs, in contrast, exhibit very rapid, analog electro-optic response, allow symmetrical driving, and no dc balance is required. VLCs are particularly attractive for applications requiring generation of multiple levels of gray scale.

## SUMMARY OF THE INVENTION

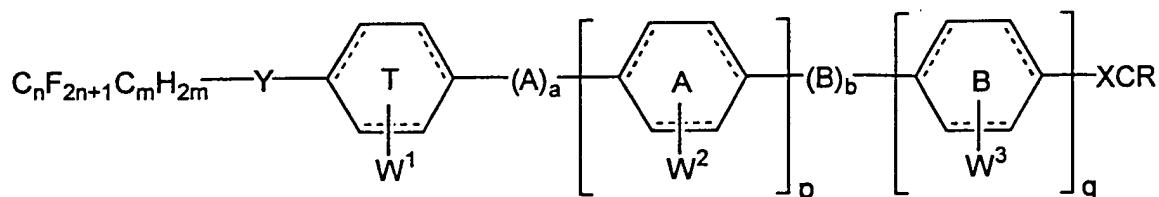
The invention relates to chiral nonracemic liquid crystal compounds having achiral tails comprising a perfluoroalkyl terminal portion which are useful as components in liquid crystal to impart high polarization to the mixture. The materials of this invention can be combined with known liquid crystal host materials to impart improved properties. Chiral nonracemic compounds of this invention can function as additives or dopants in host materials to impart chirality into an LC material.

Most generally the invention provides a method for increasing the polarization of a given FLC mixture containing a chiral nonracemic dopant by replacing the achiral tail of the chiral nonracemic dopant with an achiral tail that comprises a terminal perfluoroalkyl portion, such as an achiral tail of formula:



where Y is oxygen or a single bond and n and m are integers ranging from 1 to 20. The sum n + m is preferably 5-12. In specific embodiments n is 1, 2, 3, 4, 5, or 6 and m is 2 to 10. The enhancement of spontaneous polarization of LC mixtures containing one or more compounds of this invention is general and will apply with a variety of chiral nonracemic tail groups.

More specifically the invention relates to chiral nonracemic compounds of general formula:



wherein n and m are integers ranging from 1 to about 20;

a, b, p and q are either 0 or 1, when p is 0, a is 0 and when q is 0, b is 0;

Y is a single bond or an oxygen;

X is selected from the group consisting of a single bond, oxygen, -CO-, -O-CO-, and -CO-O-;

CR is a chiral, non-racemic tail group;

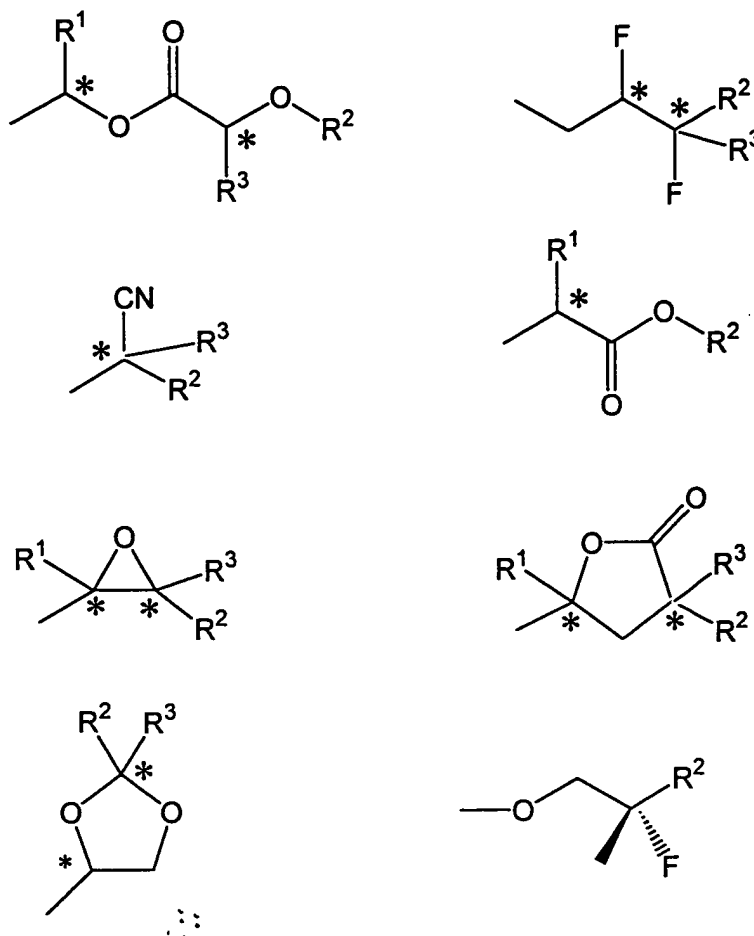
A and B, independently, are linker groups that can be selected from the group consisting of -CO-, -O-CO-, -CO-O-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -C≡C-, -C=C-, or -C=C-C=C-;

W<sup>1</sup>, W<sup>2</sup>, and W<sup>3</sup>, independently, represent one or more optional substituents on core rings which can be selected from the group consisting of H, halide, alkyl, alkoxy, haloalkyl, alkenyl, haloalkenyl, nitro, or nitrile; and

rings T, A and B together representing the mesogenic core are selected from the group of aromatic or alicyclic rings, with preferred rings being cyclohexane, cyclohexene, a phenyl, pyridine, pyrimidine or a naphthyl group, wherein one or two ring CH<sub>2</sub> groups or CH groups are replaced by -N-, S, NH, -O- or -C=O.

In a specific embodiment CR is not a chiral hydrocarbon tail;

Specific chiral tails of this invention include, among others,

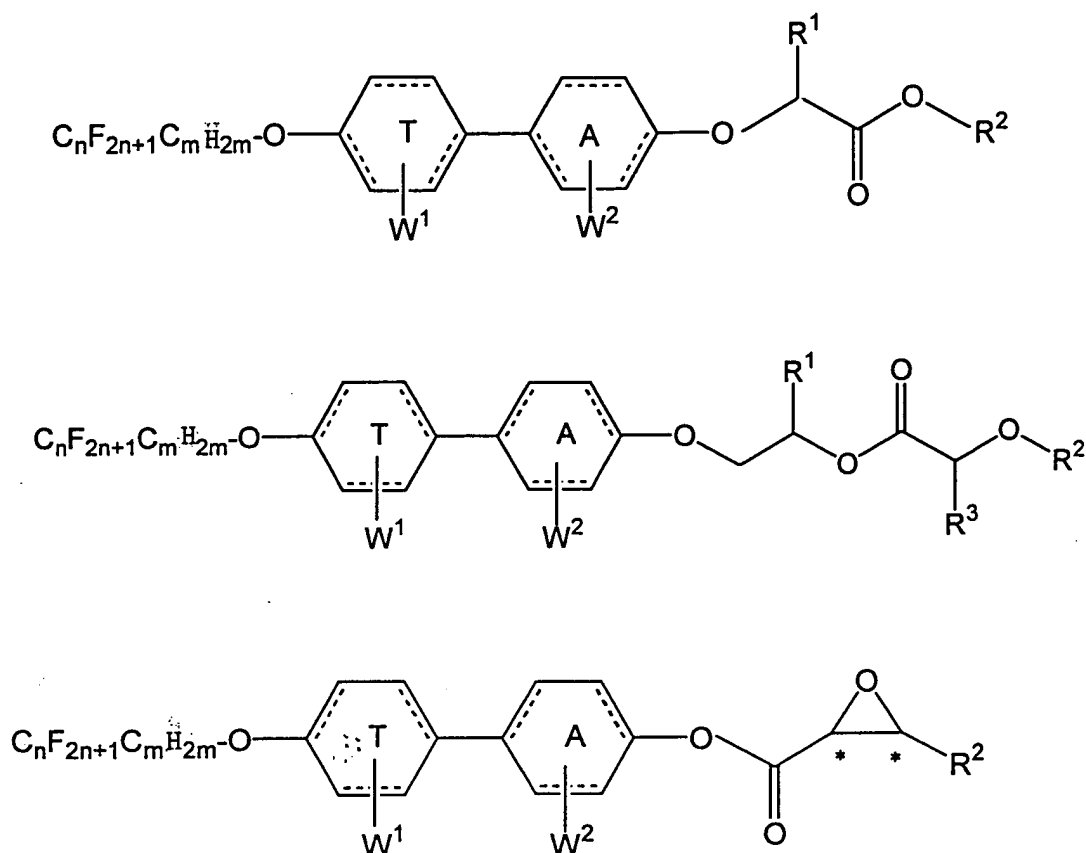


as well as  $-\text{CH}_2-(\text{C}^*\text{HF})_f-\text{R}^2$

wherein \* indicates an asymmetric carbon; f is 1, 2, or 3,  $\text{R}^1$  and  $\text{R}^3$ , independently of each other, are lower alkyl or alkenyl groups [lower alkyl having 1 to 6 carbon atoms] which are optionally substituted with one or more halogens, e.g., perfluoralkyl groups, and  $\text{R}^2$  is an alkyl, alkenyl, ether, thioether, silyl group having from 1 to about 20 carbon atoms wherein one or more  $\text{CH}_2$  groups are replaced with  $-\text{S}-$ ,  $-\text{O}-$ ,  $-\text{CO}-$ ,  $-\text{CO}-\text{O}-$ ,  $-\text{O}-\text{CO}-$ , or  $-\text{Si}(\text{R}')_2$ , and where  $\text{R}'$  is a lower alkyl optionally substituted with one or more halogens. Preferred lower alkyl groups are methyl groups.

Mesogenic cores of this invention include those of Scheme 1.

Specific compounds of this invention include:



where variable are defined above and \* indicates an asymmetric carbon.

FLC compositions of this invention include those that comprise 1 to 100% of one or more chiral nonracemic compound of this invention. Preferred compositions comprise 1 to 50% of one or more chiral nonracemic compounds of this invention. More preferred compositions comprise 1 to 25% of one or more chiral nonracemic compounds of this invention. Compositions of this invention also include those which comprise one or more chiral nonracemic

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compounds of this invention present in the composition at a level of 10% or less. FLC compositions of this invention include those which exhibit Ps of 10 nC/cm<sup>2</sup> or more, as measured by conventional methods. In particular, FLC compositions include those which exhibit Ps of 25 nC/cm<sup>2</sup> or more. Preferred FLC compositions exhibit Ps of 10 nC/cm<sup>2</sup> or more or Ps of 25 nC/cm<sup>2</sup> or more when contain 10 weight % or less (total amount) of one or more compounds of this invention. Ps is typically measured at room temperature.

Specific compounds of this invention with Ps data are provided in Table 1.

The following examples illustrate methods for synthesis of chiral nonracemic compounds of this invention. The synthesis of perfluorinated alcohols and core moieties with chiral nonracemic tails are illustrated. These materials are readily coupled to provide the compounds of this invention.

Schemes 2 and 3 illustrates a number of compounds that can be combined with the chiral nonracemic compounds of this invention to provided useful mixtures. Compounds illustrated therein can be prepared by methods that are well known in the art from readily available starting materials. Methods that are useful in the preparation of various LC compounds and FLC compounds are provided, for example in U.S. patents: 5,051,506; 5,061,814; 5,130,048; 5,167,855; 5,178,791; 5,178,793; 5,180,520; 5,271,864; 5,278,680; 5,380,460; 5,422,037; 5,453,218; 5,457,235; 5,539,555; 5,543,078; 5,585,036; 5,626,792; 5,637,256; 5,658,493; 5,753,139; 5,866,036; and 6,139,771. Each of which is incorporated by reference herein for synthetic methods applicable to the synthesis of compounds of this invention including compounds of structures 1-16 in Scheme 2. The listed patents along with U.S. patents 5,168,381 and 5,596,434 also provide detail of how LC and FLC compositions of this invention can be applied for the production of LC cells and optical devices.

Concurrently filed U.S. patent applications Attorney Docket Nos. 106-00, 86-00 and 85-00 all provide description of LC components and methods of synthesis of those components that



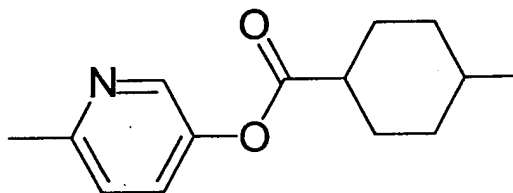
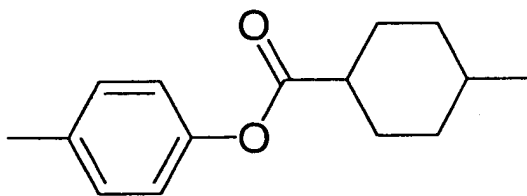
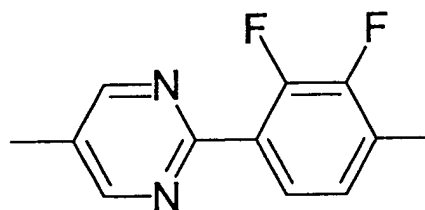
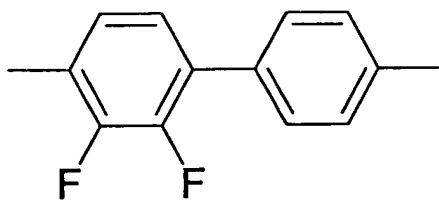
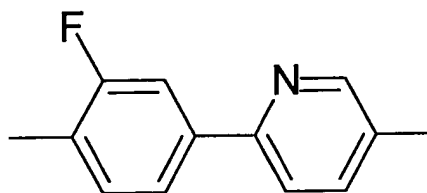
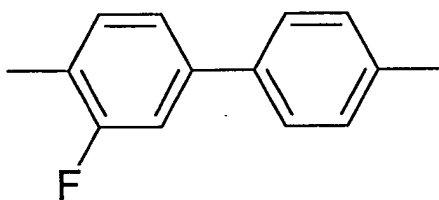
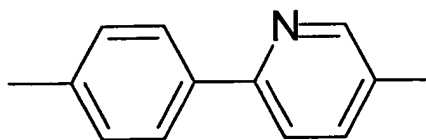
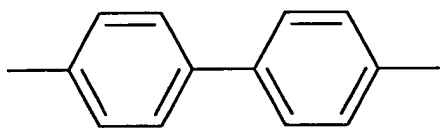
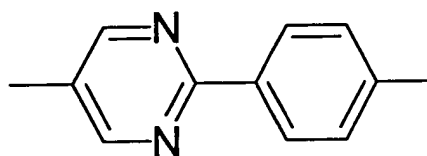
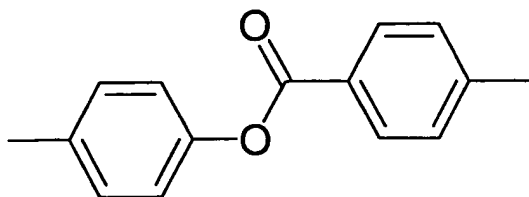
can be combined with the chiral nonracemic compounds of this invention to provide useful FLC compositions.

In addition, chiral racemic compounds or corresponding achiral compounds of this invention can be employed as additional compatible components of FLC compositions of this invention.

LC and FLCS compositions of this invention are useful in the preparation of optical devices, particularly for optical switching devices and displays. Of particular interest are SSFLC devices for use for rapid optical switching as in display applications. Those of ordinary skill in the art understand how to make LC and FLCS cells and devices that utilize the compositions of this invention. Various methods and techniques for constructing LC and FLCS cells and for use of such cells are known in the art and can be readily adapted for use with compositions of this invention. The compositions of this invention are particularly well suited for providing devices that can operate (in a smectic C phase, for example) over a broad temperature range.

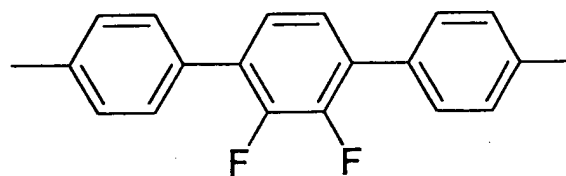
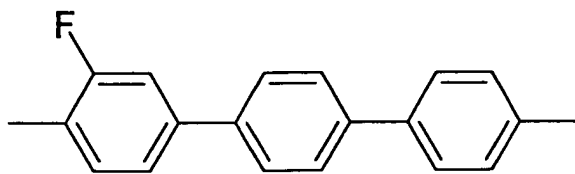
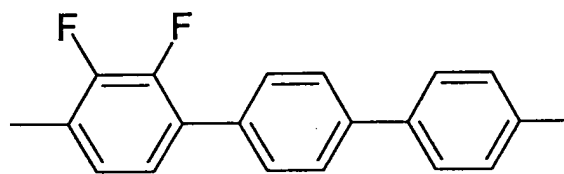
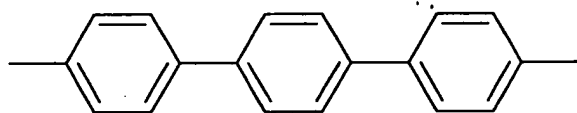
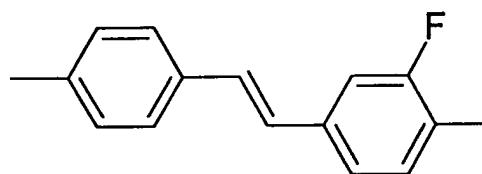
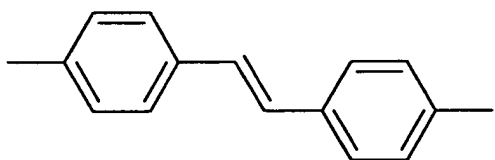
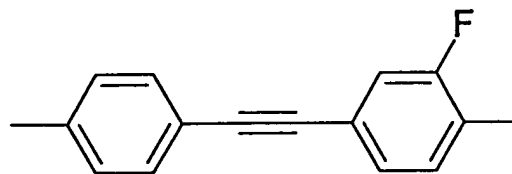
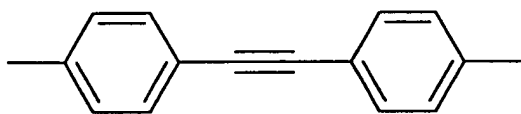
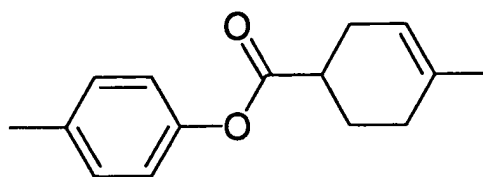
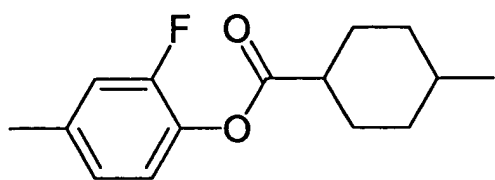
All references cited herein are incorporated by reference herein to the extent that they are not inconsistent with the disclosure herein.

SCHEME 1 (Page 1)



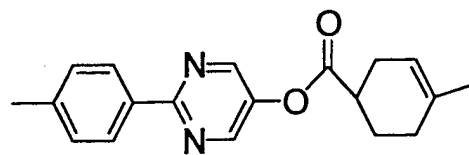
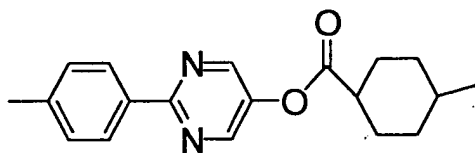
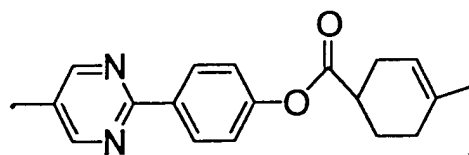
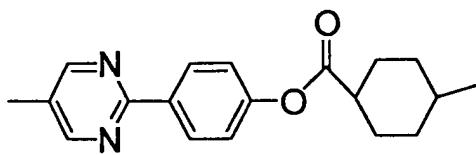
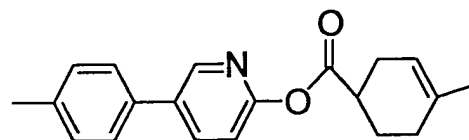
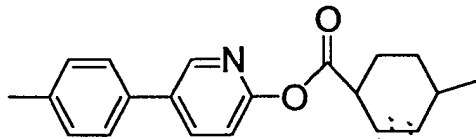
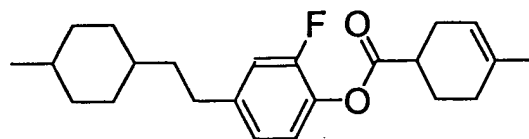
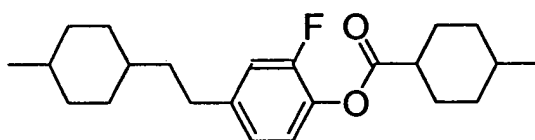
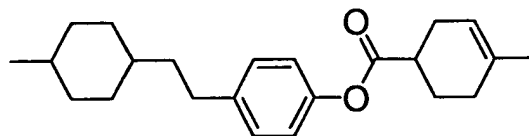
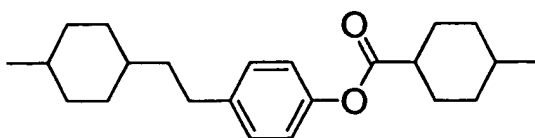
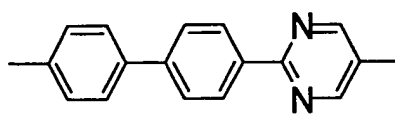
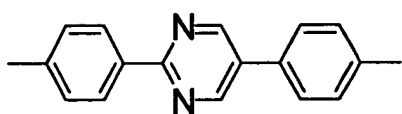
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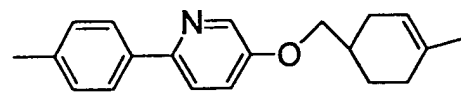
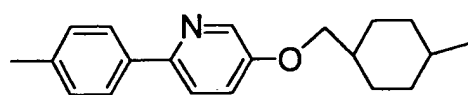
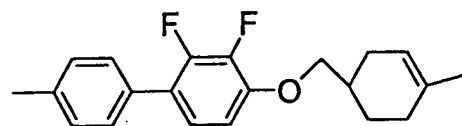
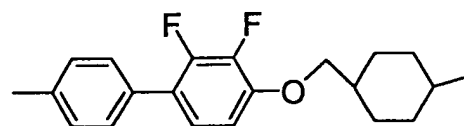
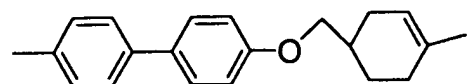
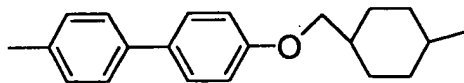
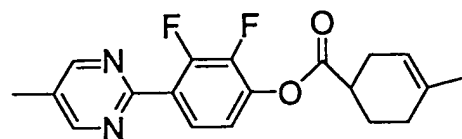
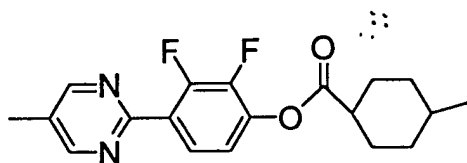
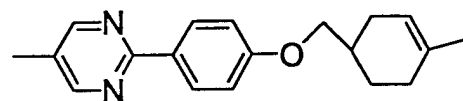
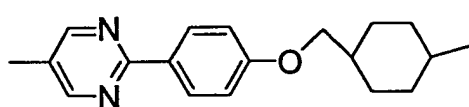
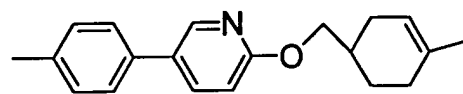
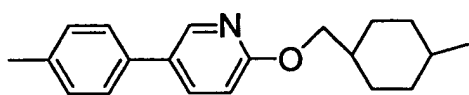
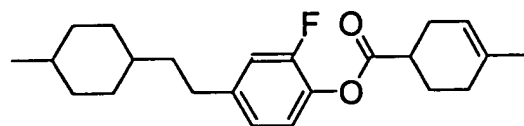
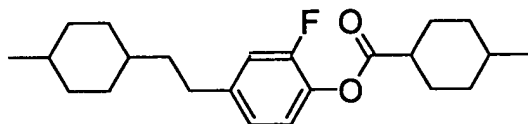
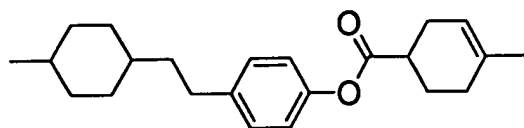
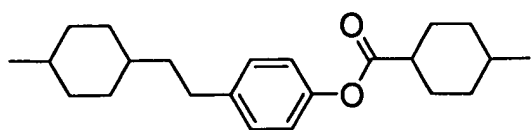
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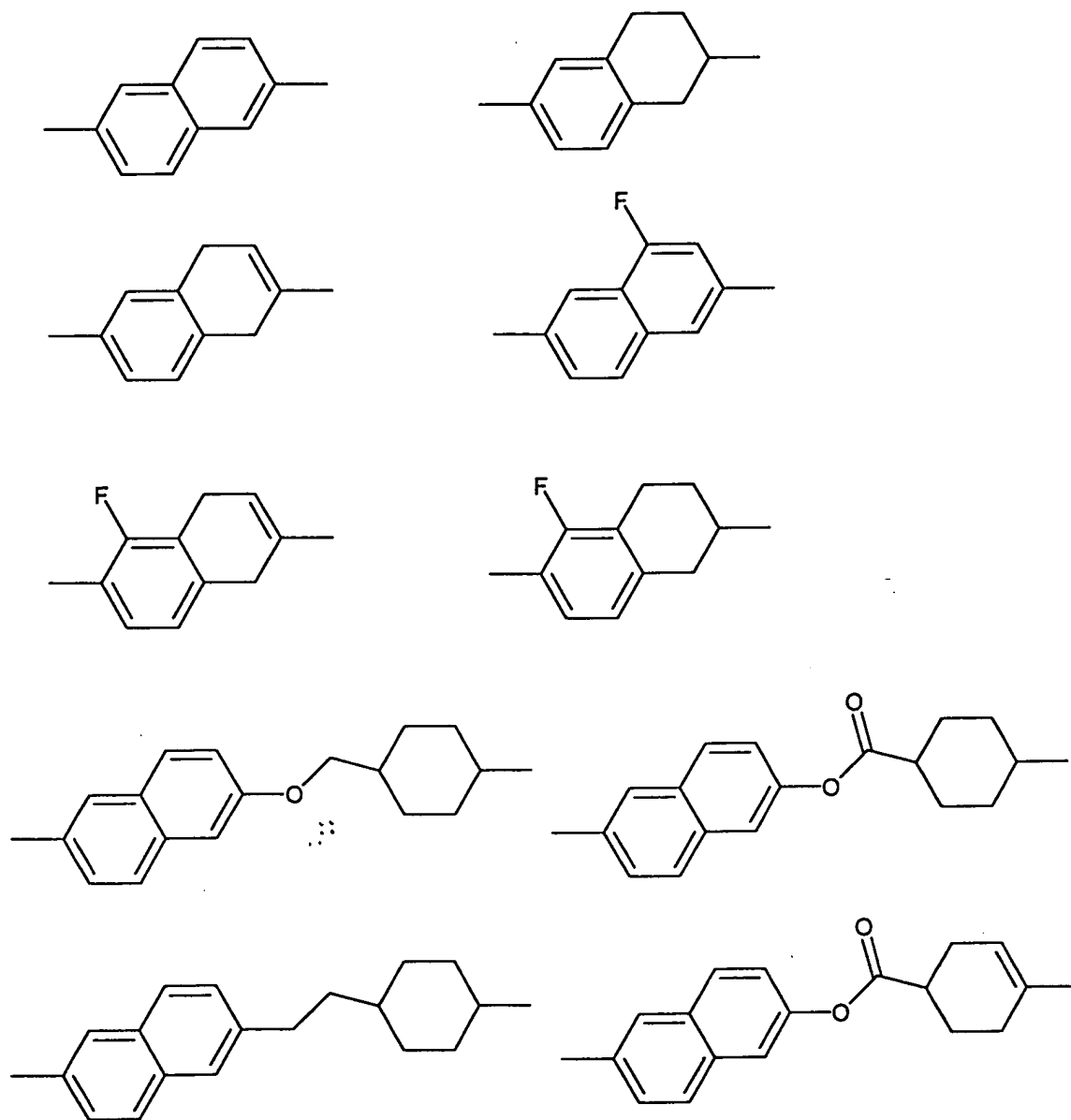
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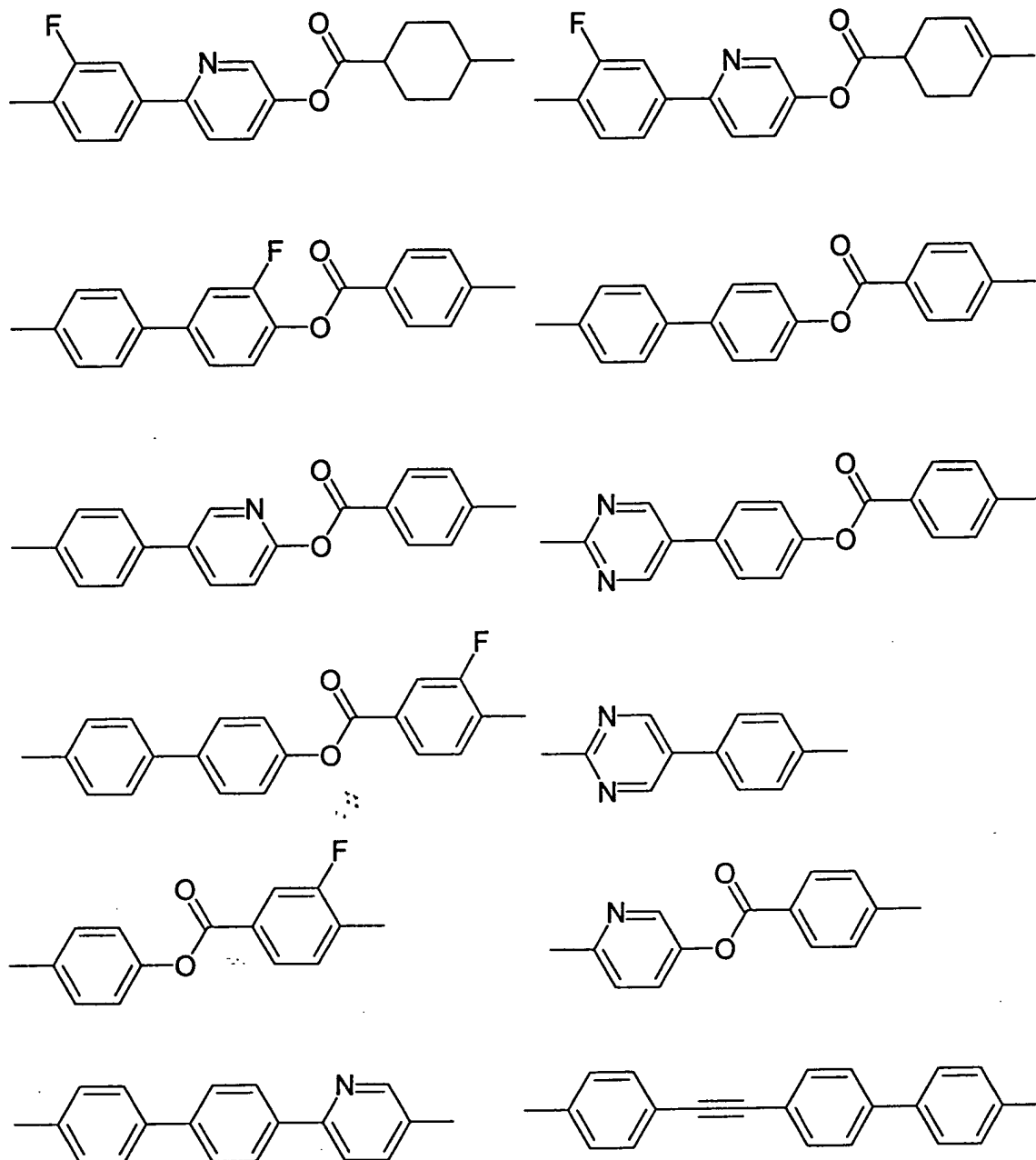


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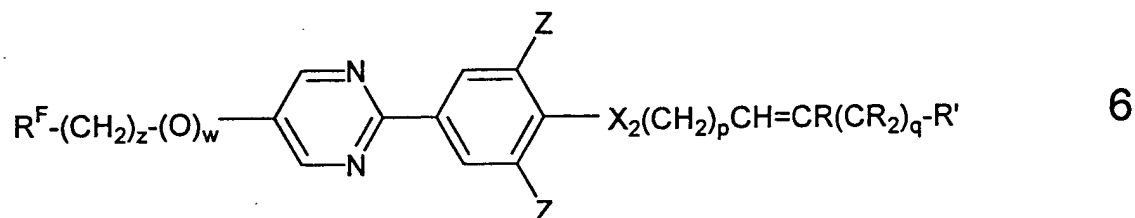
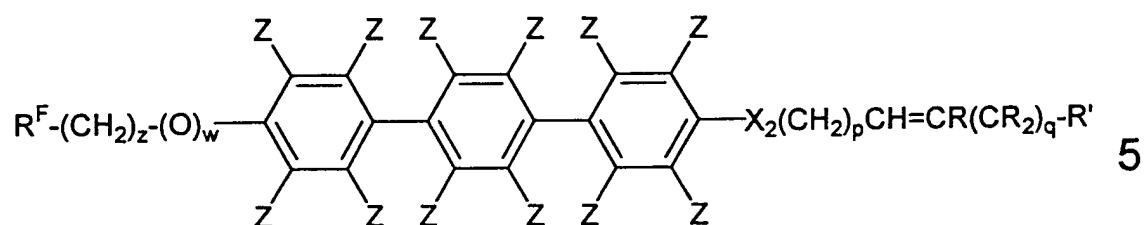
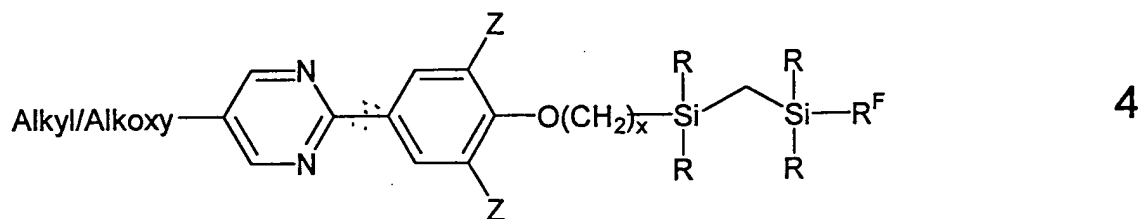
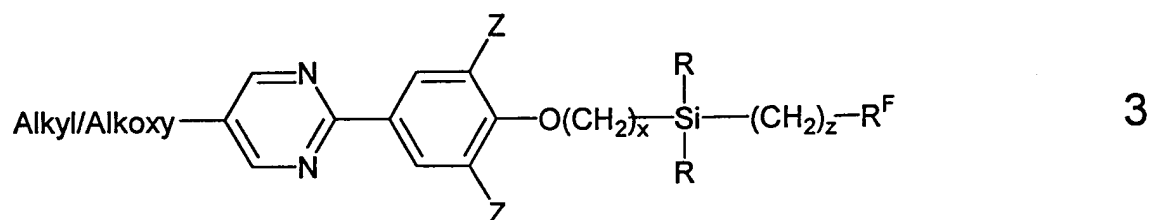
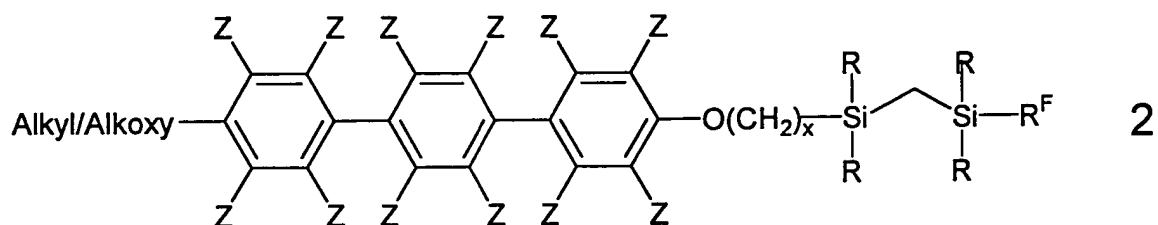
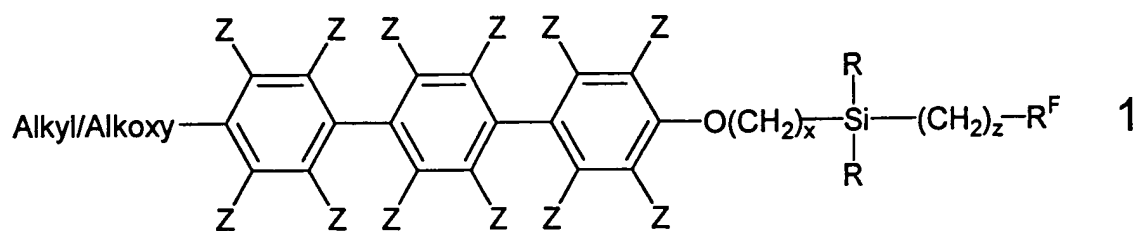


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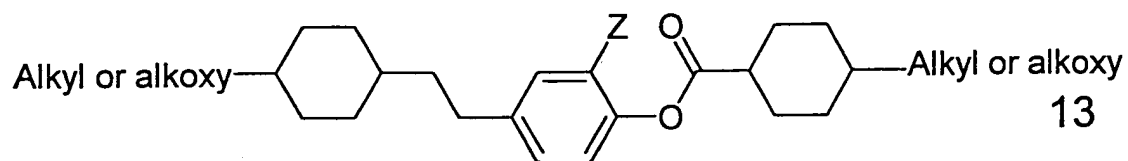
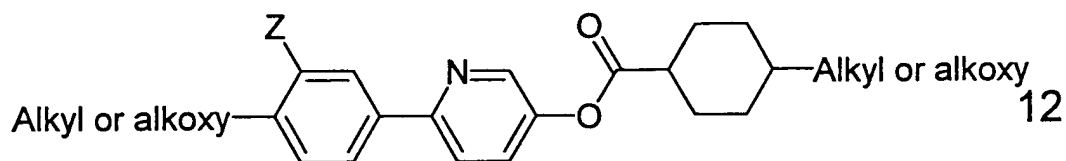
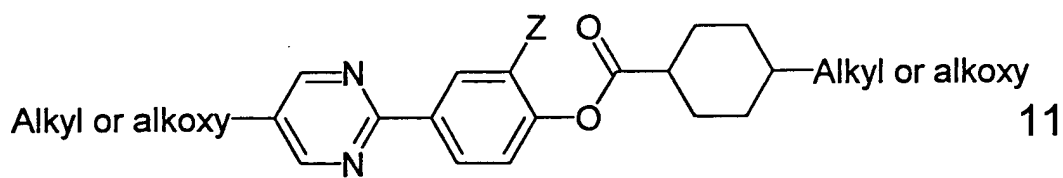
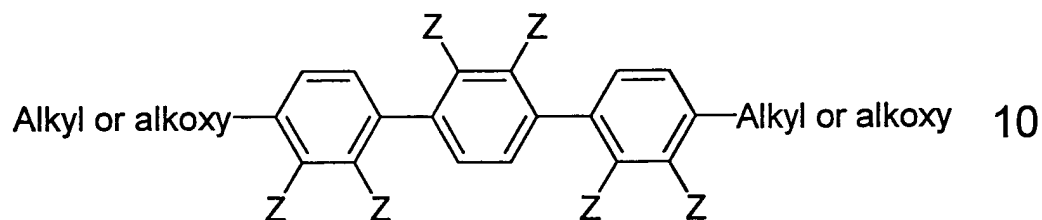
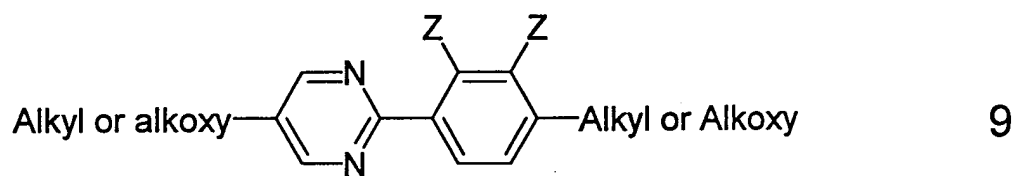
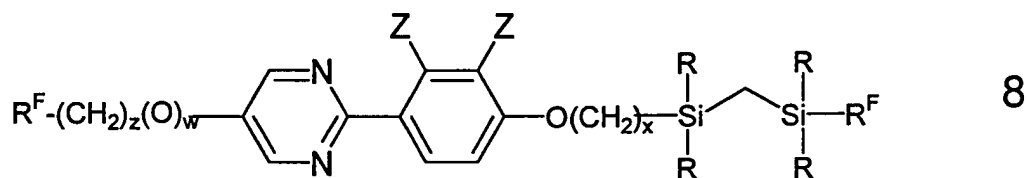
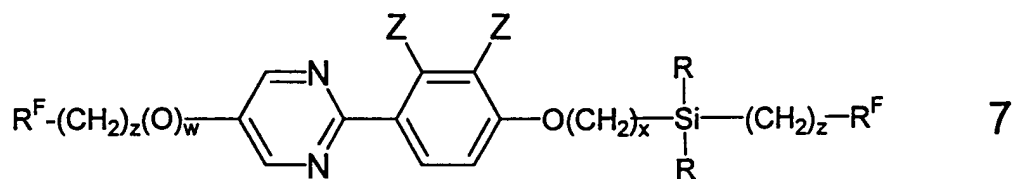
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SCHEME 2 (Page 1)

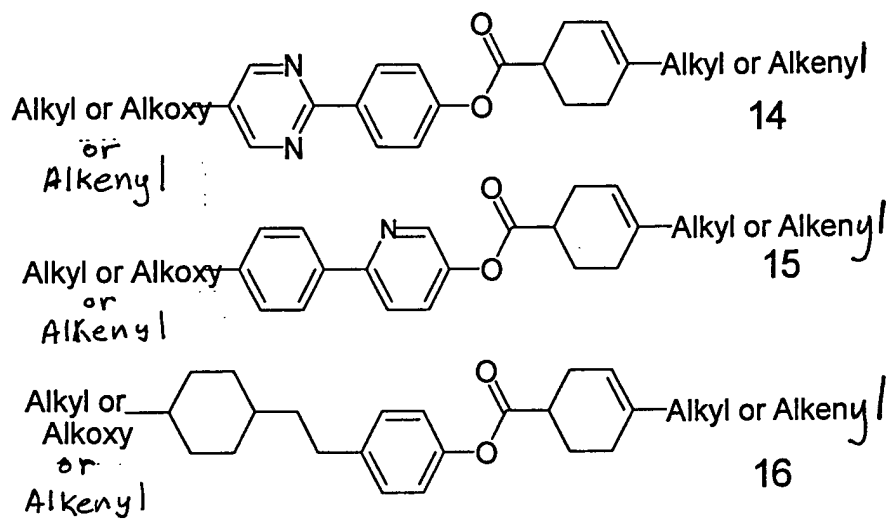




SCHEME 2 (Page 2)

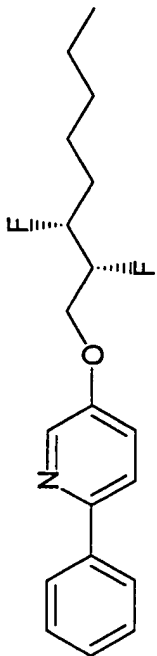
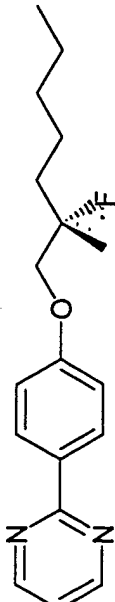
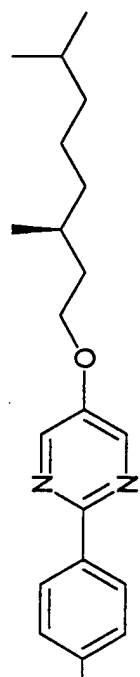
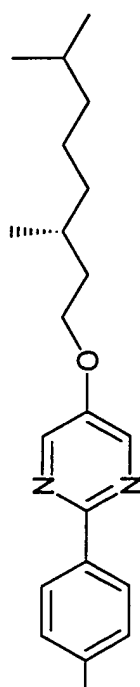
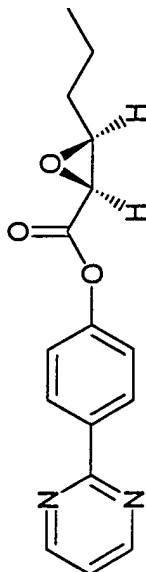


SCHEME 2 (Page 3)



wherein p, x and z are integers ranging from 1 to 20, inclusive, q is 0 or an integer ranging from 1 to 20, inclusive; y is 0 or 1; R are alkyl groups, preferably having from 1 to 6 carbon atoms; R' is an alkyl group having from 5 to 20 carbon atoms; R<sup>F</sup> is a perfluoroalkyl group; Z is H or a F; and alkyl or alkoxy groups are those that have 1 to 20 carbon atoms.

SCHEME 3 (Page 1)

| MDW # | Structure   | Phase Diagram                                       |
|-------|---|---|
| 950   |     | X <-90 - I<br>- 94->                                |
| 987   |     | X <-21----- SmC* <-54- SmA <-63-I<br>-53-> S? -57-> |
| 644   |     | X <-20- N <-41-I<br>-43-> -47->                     |
| 699   |    |   |
| 139   |  | X - 75-> I<br><-86-                                 |

SCHEME 3 (Page 2)

MDW #

Structure

Phase Diagram

|      |  |  |
|------|--|--|
| 337  |  | X < -100- C < -105- N < -169- I                      |
| 1135 |  | X < -73.5- S? < -85- C < -104- A < -175- N < -186- I |
| 1638 |  |  |
| 1458 |  |  |
| 1671 |  | X -56-> C -106-> A -131-> N -136-> I                 |
| 1673 |  | X -37-> N -112-> I<br>X < -24- C                     |
| 1674 |  | X -66-> SI -75-> C -119-> A -135-> N -137-> I        |

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SCHEME 3 (Page 3)

| MDW# | Structure | Phase Diagram                             |
|------|-----------|---|
| 31   |           |   |
| 3    |           | X -49-> A -44->N -69.5-> I                |
| 1695 |           |   |
| 5    |           | X -43.2->C -62.4->A -66.8->N<br>-68.2-> I |
| 4    |           | X -33->C -60->A -74.5-> I                 |
| 913  |           | X -43->C -50-> I<br><-44- <52-            |
| 911  |           | X -44->C -52-> I<br><-37- <-52-           |
| 374  |           |   |

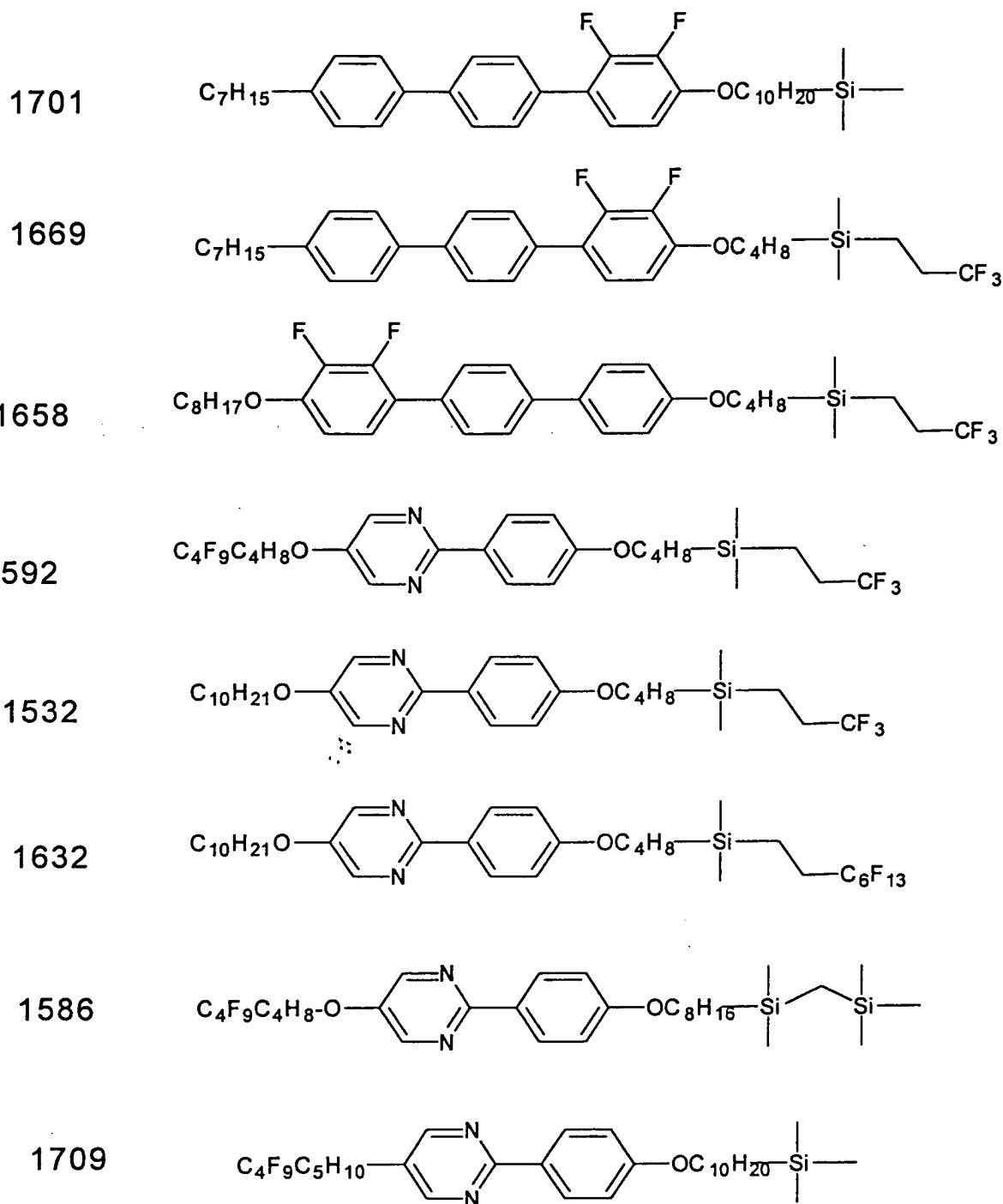
SCHEME 3 (Page 4)

| MDW  | Structure | Phase Diagram                                      |
|------|-----------|--|
| 1054 |           | X <----- C <-135- N<-150- I<br>-55-> Sx -82->      |
| 942  |           |  |
| 576  |           | X <-35- S? <-45 - C <-68- N<-107- I<br>-50-> -54-> |
| 1059 |           |  |
| 336  |           | X <-27- C <-83- N<-106- I<br>-40->                 |
| 577  |           |  |

SCHEME 3 (Page 5)

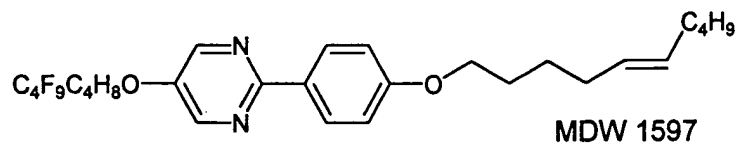
MDW#

Structure

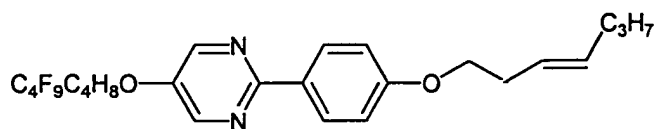


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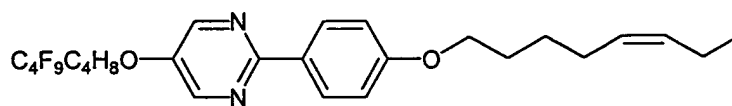
SCHEME 3 (Page 6)



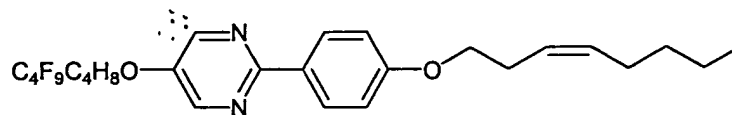
Cr 64.9 SmC 100.4 SmA 102.4 I  
43.3 99.6 101.0



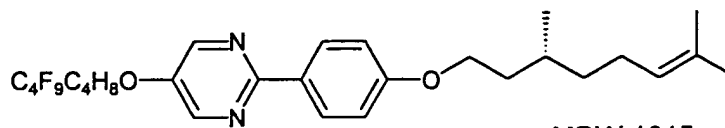
Cr 61.7 SmC 135.0 I  
57.7 134.6



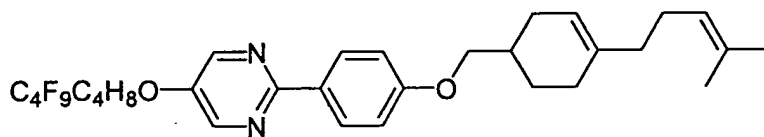
Cr 70.7 SmC 113.8 SmA 115.4 I  
60.7 113.8 114.6



Cr 59.0 SmC 114.2 SmA 121.0 I



Cr 62 SmA 67 I



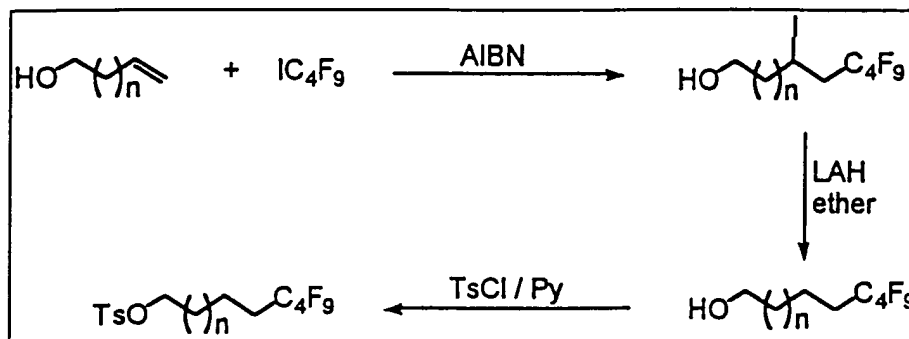


[illegible]

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|      |  |                          |      |    |
|------|--|--------------------------|------|----|
| 1195 |  | Cr 35 I                  | 0    | 10 |
| 1192 |  | Cr 86.4 I                | 0.8  | 10 |
| 1377 |  | Cr 114.5 I               | 7.25 | 10 |
| 1175 |  | Cr 124.7 I               | 9.9  | 10 |
| 1400 |  | Cr 134 I                 | 12.5 | 5  |
| 1401 |  | Cr 153 I                 | 13.5 | 5  |
| 1426 |  | Cr 119 I                 | 4.59 | 5  |
| 1427 |  | Cr 150.9 I               | 4.89 | 5  |
| 1153 |  | Cr 75 I                  | 14.5 | 10 |
| 1159 |  | Cr 79 I 87 Sx 84 Cr      | 41.4 | 10 |
| 1194 |  | Cr 37 I                  | 35   | 10 |
| 1252 |  | Cr 105 I 96 Sx 87<br>Cr  | 25   | 10 |
| 1253 |  | I 98 SA 89 Sx1 85<br>Sx2 | 17   | 10 |
| 1213 |  | Cr 79 I 74 Sx 69<br>Cr   | 34.5 | 10 |

# SYNTHETIC PROCEDURES FOR HIGH PS DOPANT



## 7,7,8,8,9,9,10,10,10-Nonafluoro-5-iodo-decanol

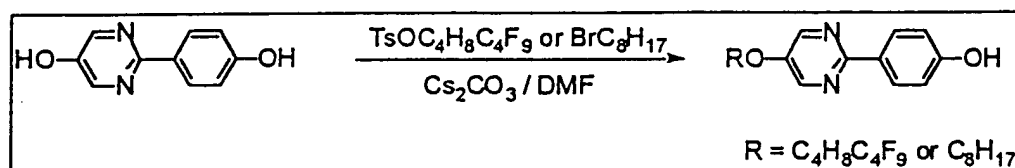
To the mixture of 5g of 5-hexenol and 17.4 g of perfluoro iodobutane, was added 110 mg of AIBN at RT under N<sub>2</sub> atmosphere. After 15 mins, another 110 mg of AIBN was added. The resulting solution was then refluxed at 70°C for 4 hrs. The reaction mixture was cooled down and used for the next reaction without further purification.

## 7,7,8,8,9,9,10,10,10-Nonafluoro-decanol

To the solution of 2 g of LAH in 120 ml of abs. ether, was added slowly ca. 22g of 7,7,8,8,9,9,10,10,10-Nonafluoro-5-iodo-decanol derivative in 30 ml abs. Ether. After addition, the reaction mixture was stirred at RT for two days and then cooled down to 5°C in the ice water. Water was added slowly until no gas evolved. The solid was filtered through short column of silica gel, washed with ether and ethyl acetate. The filtrate was combined and the solvent was evaporated. The residue was distilled under vacuum to give 13 g (81% yield) of the partial-fluoro alcohol.

## 7,7,8,8,9,9,10,10,10-Nonafluoro-decyl tosylate

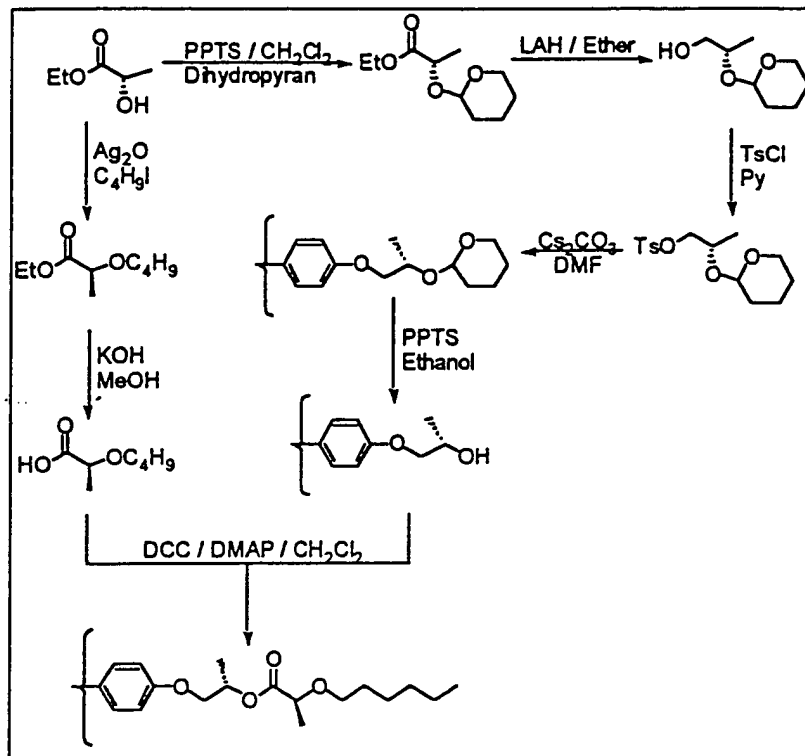
The solution of 9.8g of partial-fluoro alcohol in 40 ml of pyridine was cooled down to 0°C in ice-salt water and 6 g of TsCl was added in small portion. After addition the resulting mixture was stirred at 0°C for two hours and then placed in freezer (-20°C) for two days. The reaction mixture was poured into ice water and the product was extracted with ethyl acetate twice. The combined organic phase was washed with brine, 10% HCl and again brine three times, and then dried over MgSO<sub>4</sub>. After evaporation of solvent, pure partial-fluoro tosylate was obtained in yield of 98%.



## 4-(2-(5-alkoxy)pyrimidin-5-yl)phenol

25 mmol of alkyl tosylate or bromide, 25 mmol of pyrimidylphenol derivative, 30 mmol of Cs<sub>2</sub>CO<sub>3</sub> and 50 ml of DMF were mixed together and stirred at RT over night. The reaction mixture was then poured into water. The solid was filtered and washed with

2.2 mmol of benzoate derivative, 3 g of KOH and 60 MeOH were stirred at 70°C over night. Then MeOH was removed and the residue is mixed with water and neutralized with conc.HCl. The solid was collected, washed with water and dried under vacuum. The yield is 95%.



#### Ethyl [S]-tetrahydropyranyloxy propionate

10 g of L-ethyl lactate, 8.5 g of 3,4-dihydro-2H-pyran, 0.5g PPTS and 150 ml of methylene chloride were put together and stirred at RT for two days. The excess solvent was removed and the residue was mixed with 80/20 hexane and ethyl acetate. The solid was filtered and the solution was concentrated. The residue was further purified by flash chromatography to give pure product. The yield was 88%.

#### [S]-2-tetrahydropyranyloxy-1-propanol

4.1g of THP protected lactate in 80 ml of dry ether was added to a mixture of 2 g of LiAlH<sub>4</sub> in 120 ml of dry ether. The addition was controlled to keep a gentle reflux. After addition, the reaction mixture was stirred at RT for 3 hrs and 10 ml of water was added with great care. The mixture was then filtered through a short column of silica gel and washed with ether. The solvent was evaporated to give pure product (yield ~100%).

#### [S]-2-tetrahydropyranyloxy-1-propyltosylation

The solution of 3.2g of [S]-2-tetrahydropyranyloxy-1-propanol in 30 ml of pyridine was cooled down to 0°C in ice-salt water and 3.5 g of TsCl was added in small portion. After addition the resulting mixture was stirred at 0°C for two hours and then placed in freezer (-20°C) for two days. The reaction mixture was poured into ice water and the product was extracted with ethyl acetate twice. The organic phase was washed with brine, 10% HCl,

diluted  $\text{Na}_2\text{CO}_3$  and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was purified by flash chromatography to give 6g of tosylate (yield 95%).

[S]-2-tetrahydropyranyloxy-1-propoxyphenyl derivative

2.1 mmol of Tosylate, 2 mmol of phenol, 2 mmol of  $\text{Cs}_2\text{CO}_3$  and 20ml of DMF were put together and stirred at RT over night. Then the reaction mixture was poured into water and the product was collected by extraction. The organic solution was washed with brine and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was purified by flash chromatography to give pure product with yield of over 95%.

[S]-2-hydroxy-1-propoxyphenyl derivative

0.6 g of [S]-2-tetrahydropyranyloxy-1-propoxyphenyl derivative, 0.1 g of PPTS and 20 ml of ethanol were stirred at  $95^\circ\text{C}$  for 3hrs and then the ethanol was removed. The residue was mixed with ethyl acetate and filtered through short column silica gel, washed with ethyl acetate. The combined filtrate was evaporated to dryness to give pure product (yield 82%).

Ethyl [S]-2-methyl-3-oxo-heptanoate

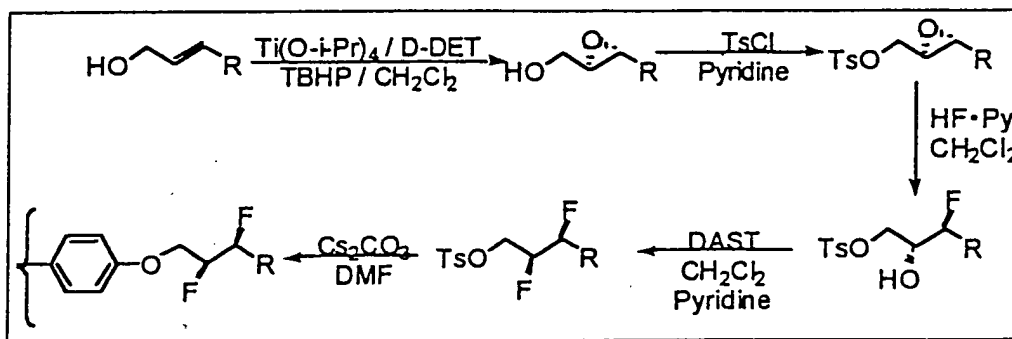
1.5g of L-ethyl lactate, 4.5g of  $\text{Ag}_2\text{O}$  and 15 ml of iodobutane were mixed together and stirred at  $40^\circ$  over night. The black solid was filtered out and the filtrate was distilled to give 1.4g of product (yield 65%).

[S]-2-methyl-3-oxo-heptanoic acid

1g of Ethyl [S]-2-methyl-3-oxo-heptanoate, 0.5g of KOH and 15 MeOH were stirred at  $50^\circ\text{C}$  for 4 hrs. Then MeOH was removed and the residue is mixed with water, neutralized with conc.HCl and extracted with methylene chloride. The combined organic phase was washed with water for 3-4 times and dried over  $\text{MgSO}_4$ . After evaporation of solvent, 0.8 g of product was obtained (yield 95%).

[S,S]-1-Phenoxy-2-propyl 2-methyl-3-oxo-heptanoate derivative

80 mg of [S]-2-methyl-3-oxo-heptanoic acid, 150 mg of [S]-2-hydroxy-1-propoxyphenyl derivative, 160mg of DCC, 10mg of DMAP and 20ml of methylene chloride were put together and stirred at RT over night. The solid was filtered out and the filtrate was concentrated. The residue was purified by flash chromatography to give pure product with yield over 80%.



(2S, cis)-3-propyloxiranemethanol

To the mixture of 210ml methylene chloride and 4g of activated 4Å powder sieves, cooled to -20°C, 1.5g of L-(+) diethyl tartrate and 1.5g of  $\text{Ti}(\text{O}-i\text{-Pr})_4$  was added with stirring. Then 20 ml of TBHP in methylene chloride (ca. 5-6 M) was added through addition funnel at a moderate rate (ca. 5 minutes). The resulting mixture was stirred at -20°C for 30 minutes and 5 g of cis-3-hexene-1-ol in 25 ml of methylene chloride was added dropwise over period of 20 mins. The temperature was kept between -15 to -20°C. The stirring was continued for another hour and then stored in freezer (-20°C) for two days. After warmed up to 0°C, 30 ml of water was added and the mixture is stirred for 1 hour, while allowing it to warm up to RT. 6 ml of 30% aqueous solution of NaOH saturated with NaCl was added and stirred vigorously. After 20 mins, there was a phase separation. The bottom organic phase was removed and top aqueous phase was extracted with methylene chloride. The combined organic phase was then dried and the solvent was removed. The residue is further purified by distillation to give pure product with yield of 75%.

(2S, cis)-3-propyloxiranemethyl tosylate

The solution of 1g of (2S, cis)-3-propyloxiranemethanol in 10 ml of pyridine was cooled down to 0°C in ice-salt water and 4.5 g of TsCl was added in small portion. After addition the resulting mixture was stirred at 0°C for one hours and then placed in refrigerator (5°C) for three days. The reaction mixture was poured into ice water and the product was extracted with ether. The combined organic phase was washed with 15% HCl cold solution, saturated  $\text{NaHCO}_3$  and brine, and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was further purified by flash chromatography to give 2.4g of tosylate (yield 97%).

(2S, 3R)-3-fluoro-2-hydroxyhexyl tosylate

To the solution of 18.5 mmol of tosylate in 180 ml methylene chloride, cooled in dry ice-acetone, was added 5.7 ml of HF/Py. After addition the reaction solution was allowed to warm up slowly to -50°C (it took about 2 hrs) and placed in freezer (-25°C) over night. Then it was poured into water. Separated the organic phase, followed by washed with  $\text{NaHCO}_3$  and water. Dried over  $\text{MgSO}_4$ . After evaporation of solvent, an oil product was obtained, which was used directly for the next reaction (yield 110%).

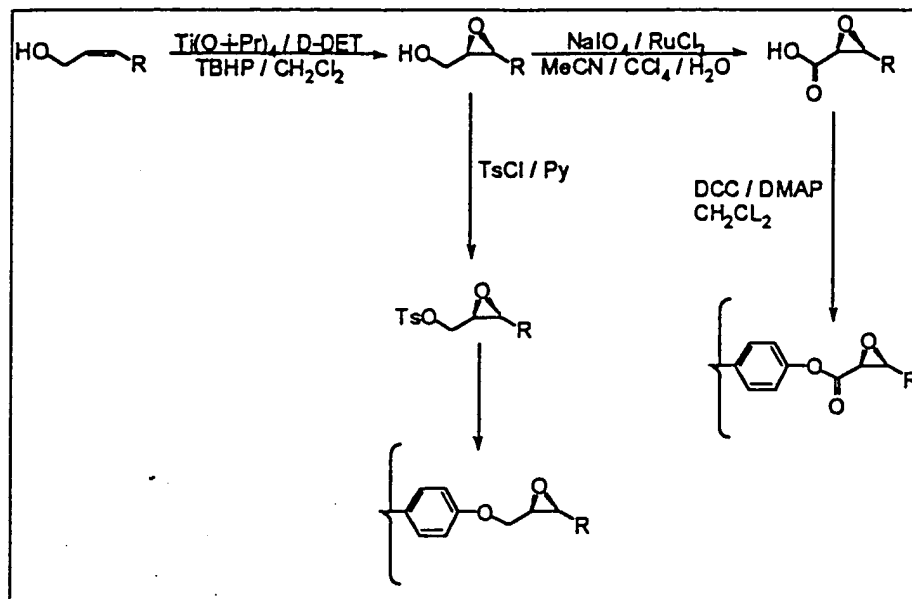
(2R, 3R)-2,3-difluorohexyl tosylate

To the solution of 0.71 mmol of monohydroxy derivative in 30 ml of methylene chloride, cooled down to -78°C, was added 0.4 ml of DAST. After addition, the reaction solution was allowed to warm up to RT slowly and stirred at RT over night. Then it was poured into water, extracted with ethyl acetate, washed with brine and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was purified by flash chromatography. Yield is 50%.

(2R, 3R)-2,3-difluorohexylox phenyl derivative

2.1 mmol of Tosylate, 2 mmol of phenol, 2 mmol of  $\text{Cs}_2\text{CO}_3$  and 20ml of DMF were put together and stirred at RT over night. Then the reaction mixture was poured into water and the product was collected by extraction. The organic solution was washed with brine

and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was purified by flash chromatography to give pure product with yield over 95%.



#### (2S, cis)-3-propyloxiranemethanol

To the mixture of 210ml methylene chloride and 4g of activated 4Å powder sieves, cooled to  $-20^\circ\text{C}$ , 1.5g of L-(+) diethyl tartrate and 1.5g of  $\text{Ti(O-}i\text{Pr)}_4$  was added with stirring. Then 20 ml of TBHP in methylene chloride (ca. 5-6 M) was added through addition funnel at a moderate rate (ca. 5 minutes). The resulting mixture was stirred at  $-20^\circ\text{C}$  for 30 minutes and 5 g of cis-3-hexene-1-ol in 25 ml of methylene chloride was added dropwise over period of 20 mins. The temperature was kept between  $-15$  to  $-20^\circ\text{C}$ . The stirring was continued for another hour and then stored in freezer ( $-20^\circ\text{C}$ ) for two days. After warmed up to  $0^\circ\text{C}$ , 30 ml of water was added and the mixture is stirred for 1 hour, while allowing it to warm up to RT. 6 ml of 30% aqueous solution of NaOH saturated with NaCl was added and stirred vigorously. After 20 mins, there was a phase separation. The bottom organic phase was removed and top aqueous phase was extracted with methylene chloride. The combined organic phase was then dried and the solvent was removed. The residue is further purified by distillation to give pure product with yield of 75%.

#### (2S, cis)-3-propyloxiranecarboxylic acid

A flask was charged with 34 ml of  $\text{CCl}_4$ , 34 ml of acetonitrile and 2 g of (2S, cis)-3-propyloxiranemethanol. Then 11g of  $\text{NaIO}_4$  in 51 ml of water were added, followed by 86mg of  $\text{RuCl}_3$  to this biphasic solution. The mixture was stirred vigorously for 3 hrs at RT and 100 ml of methylene chloride was added. The organic phase was separated and water phase was extracted with methylene chloride. The combined black organic phase was dried over  $\text{MgSO}_4$  and concentrated. The residue was diluted with ether and filtered through celite to give colorless solution. After evaporation of solvent a pure product was obtained (yield 67%).

#### (2S, cis)-3-propyloxiranemethyl tosylate

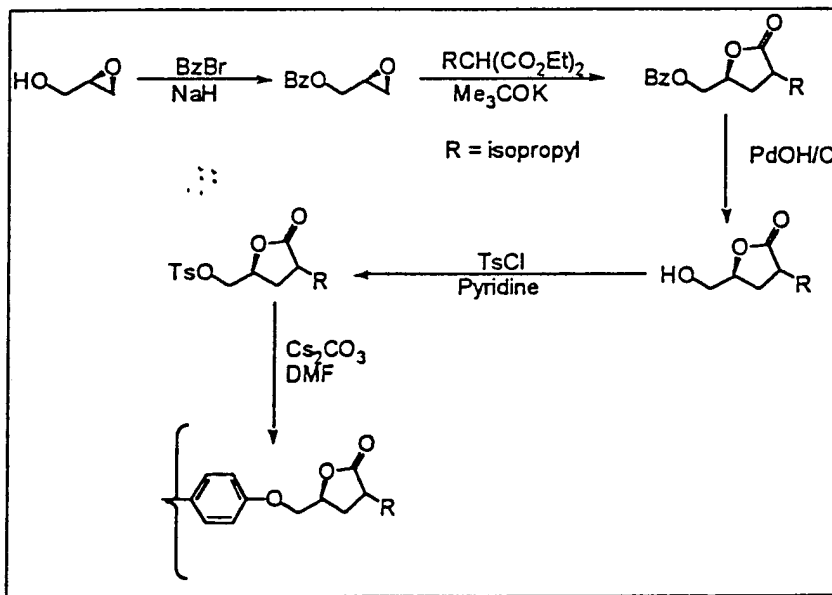
The solution of 1g of (2S, cis)-3-propyloxiranemethanol in 10 ml of pyridine was cooled down to 0°C in ice-salt water and 4.5 g of TsCl was added in small portion. After addition the resulting mixture was stirred at 0°C for one hours and then placed in refrigerator (5°C) for three days. The reaction mixture was poured into ice water and the product was extracted with ether. The combined organic phase was washed with 15% HCl cold solution, saturated NaHCO<sub>3</sub> and brine, and dried over MgSO<sub>4</sub>. After evaporation of solvent, the residue was further purified by flash chromatography to give 2.4g of tosylate (yield 97%).

#### Phenyl (2S, cis)-3-propyloxiranecarboxylate derivative

200 mg of (2S, cis)-3-propyloxiranecarboxylic acid, 0.9 equivalent of phenol derivatives, 300mg of DCC, 15mg of DMAP and 20ml of methylene chloride were put together and stirred at RT over night. The solid was filtered out and the filtrate was concentrated. The residue was purified by flash chromatography to give pure product with yield over 80%.

#### (2S, cis)-3-propyloxiranemethoxy phenyl derivative

2.1 mmol of Tosylate, 2 mmol of phenol, 2 mmol of Cs<sub>2</sub>CO<sub>3</sub> and 20ml of DMF were put together and stirred at RT over night. Then the reaction mixture was poured into water and the product was collected by extraction. The organic solution was washed with brine and dried over MgSO<sub>4</sub>. After evaporation of solvent, the residue was purified by flash chromatography to give pure product with yield over 95%.



#### [R]-3-Benzoyloxy propylene oxide

To the mixture of 1.65g of NaH in 150 ml of THF, 5 g of [R]-glycidol in 5 ml of THF was added. After stirring at RT for 10 mins, 12 g of benzyl bromide was added and the resulting mixture was stirred at RT for 3 hours. It was then hydrolyzed carefully with water and most of THF was removed. The rest was mixed with water and extracted with ethyl acetate. The organic solution was washed with brine and dried over MgSO<sub>4</sub>. After evaporation of solvent the residue was purified by flash chromatography. Yield is 54%



[R]-5-benzyloxymethyl-3-isobutyl-2(5H)-furanone

To the solution of 11 g of potassium t-butoxide in 60 ml of t-butanol, was added 2 g of [R]-3-Benzoyloxy propylene oxide, followed by 20 g of diethyl isobutyl malonate. The resulting mixture was refluxed for 15 hrs. The t-butanol was removed by distillation and the residue was poured into water. The crude product was collected by extraction with ethyl acetate. The organic phase was washed with brine and dried over MgSO<sub>4</sub>. After evaporation of solvent, the residue was distilled to remove excess diethyl isobutyl malonate and the rest was further purified by flash chromatography. Yield is 72%.

[R]-5-hydroxymethyl-3-isobutyl-2(5H)-furanone

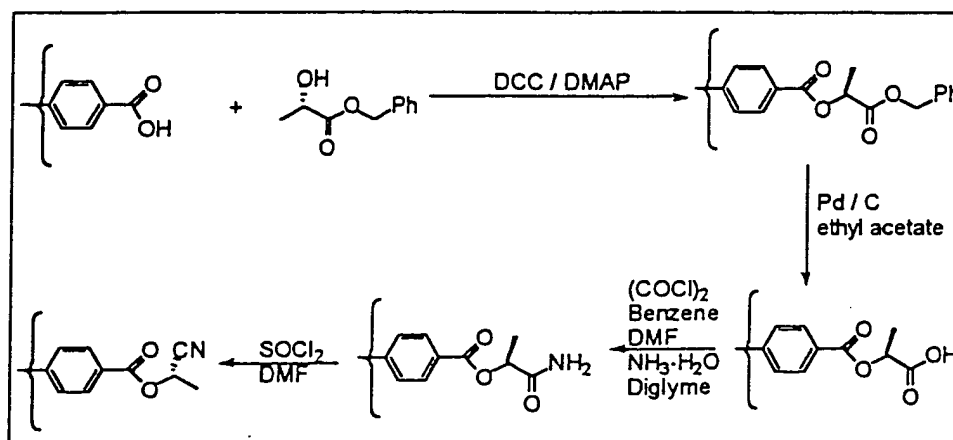
2.3 g of [R]-5-benzyloxymethyl-3-isobutyl-2(5H)-furanone, 150 mg of PdOH/C in 50 ml of ethanol was stirred at RT over night under H<sub>2</sub> atmosphere. Then the catalyst was filtered out and filtrate was evaporated to dryness to give the pure compound in yield of 99%.

[R]-5-Tosylmethyl-3-isobutyl-2(5H)-furanone

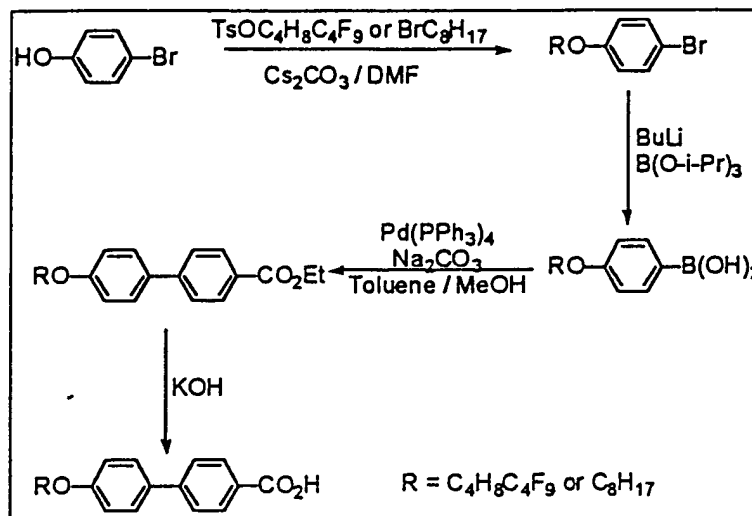
The solution of 1.5g of [R]-5-hydroxymethyl-3-isobutyl-2(5H)-furanone in 10 ml of pyridine was cooled down to 0°C in ice-salt water and 1.7 g of TsCl was added in small portion. After addition the resulting mixture was stirred at 0°C for two hours and then placed in freezer (-20°C) for two days. The reaction mixture was poured into ice water and the product was extracted with ethyl acetate twice. The organic phase was washed with brine, 10% HCl, diluted Na<sub>2</sub>CO<sub>3</sub> and dried over MgSO<sub>4</sub>. After evaporation of solvent, the residue was purified by flash chromatography to give 6g of tosylate (yield 95%).

[R]-5- phenoxy methyl-3-isobutyl-2(5H)-furanone derivative

2.1 mmol of [R]-5-Tosylmethyl-3-isobutyl-2(5H)-furanone, 2 mmol of phenol derivative, 2 mmol of Cs<sub>2</sub>CO<sub>3</sub> and 20ml of DMF were put together and stirred at RT over night. Then the reaction mixture was poured into water and the product was collected by extraction. The organic solution was washed with brine and dried over MgSO<sub>4</sub>. After evaporation of solvent, the residue was purified by flash chromatography to give pure product with yield over 95%.



water. The crude product was dissolved in ethyl acetate, washed with water and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was purified by flash chromatography. The yield is 65%.



#### 4-Alkoxy-1-bromobenzene

25 mmol of tosylate or bromide, 25 mmol of 4-bromophenol, 30 mmol of  $\text{Cs}_2\text{CO}_3$  and 50 ml of DMF were mixed together and stirred at RT over night. The reaction mixture was then poured into water and the solid was collected by extraction with ethyl acetate. The organic phase was washed with water and dried over  $\text{MgSO}_4$ . After evaporation of solvent, pure product was obtained in yield of 100%.

#### 4-Alkoxyphenylboronic acid

To the dry flask containing 37 mmol of 4-Alkoxy-1-bromobenzene and 80 ml of THF, cooled to  $-78^\circ\text{C}$ , 21 ml of BuLi (2.2M in Hexane) was added slowly. After addition the reaction mixture was stirred at  $-70^\circ\text{C}$  for 1 Hour and then 17.6 ml of triisopropylborate was added slowly. Reaction solution was allowed to warm up to RT and stirred at RT over night. Then 70 ml of water was added slowly and stirred at RT for two hours. The product was collected by extraction with hexane. The extract was washed with brine and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was purified by short column chromatography to give pure product in yield of 92%.

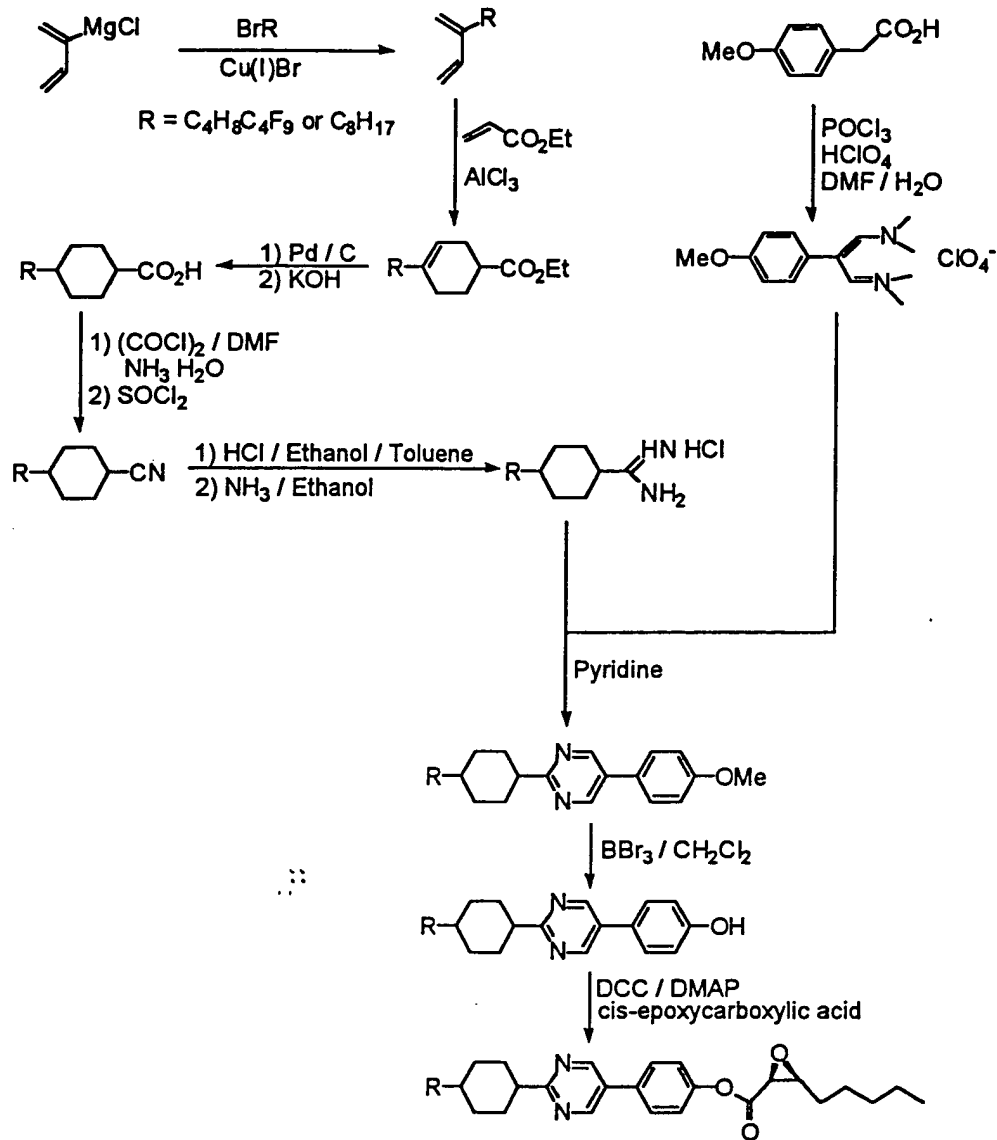
#### Ethyl 4-alkoxyphenylbenzoate

To the solution of 1.2 g of ethyl 4-bromobenzoate in 12.5 ml of toluene, was added 6 ml of  $\text{Na}_2\text{CO}_3$  (2M aqueous solution), followed by 6 mmol of boronic acid in 3 ml of methanol and 200 mg of  $\text{Pd(PPh}_3)_4$ . The resulting mixture was heated up to  $80^\circ\text{C}$  and stirred at this temperature vigorously for 48 hrs. It was then cooled down and partitioned between 30 ml methylene chloride and 25 ml of 2M aqueous  $\text{Na}_2\text{CO}_3$ . The organic phase was separated, washed with brine and dried over  $\text{MgSO}_4$ . After evaporation of solvent, the residue was purified by flash chromatography. The yield is 86%.

#### 4-alkoxyphenylbenzoic acid

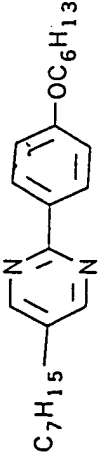
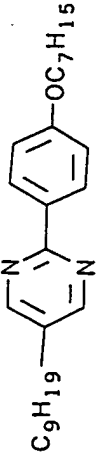
is prepared by conventional methods as illustrated above.

# Synthetic scheme for three-ring compounds

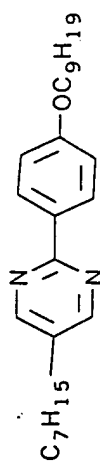
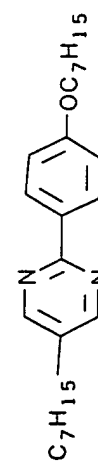



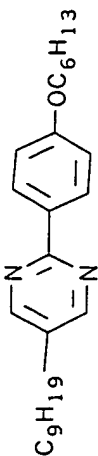
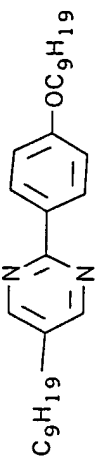
10078054-010303

Table 2 Composition of MX 6111

| MX 6111   |     |
|---|-----|
| Structure and MDW #   | %   |
| <p data-bbox="505 1167 532 1272">MDW 1</p> <div data-bbox="602 1024 699 1476">  <chem>CCCCCCCCc1ccncc1C1=CC=C(C=C1)OC2=CC=CC=C2</chem> </div>  | 5.6 |
| <p data-bbox="824 1167 852 1272">MDW 2</p> <div data-bbox="919 961 1016 1413">  <chem>CCCCCCCCCc1ccncc1C1=CC=C(C=C1)OC2=CC=CC=C2</chem> </div> | 5.6 |

|  |            |
|--|------------|
| <p>MDW 3</p> <div data-bbox="457 982 555 1432"> <chem>CCCCCCCCc1ccc(cc1)-c2cc(CCCCCC)ncn2</chem> </div>    | <p>5.6</p> |
| <p>MDW 4</p> <div data-bbox="852 982 950 1432"> <chem>CCCCCCCCCc1ccc(cc1)-c2cc(CCCCCCCC)ncn2</chem> </div> | <p>7.2</p> |

|         |  |     |
|---------|--|-----|
| MDW 22  |  <chem>CCCCCCCCc1ccncc1C1=CC=C(C=C1)OC(C)(C)CCCCCCC</chem>               | 5.6 |
| MDW 31  |  <chem>CCCCCCCCc1ccncc1C1=CC=C(C=C1)OC(C)(C)CCCCC</chem>                 | 5.6 |
| MDW 343 |  <chem>CCCCCCCCc1ccncc1C2=CC=CC=C2OC3CCNCC3C4=CC=C(C=C4)C=C(C)C</chem> | 20  |

|          |  |      |
|----------|--|------|
| MDW 764  |  <chem>CCCCCCCCCc1ccncc1Oc2ccc(cc2)</chem> | 9.6  |
| MDW 1287 |  <chem>CCCCCCCCCc1ccncc1Oc2ccc(cc2)</chem> | 33.6 |